

### **REMARKS**

The Application has been reviewed in light of the Office Action mailed May 28, 2003. At the time of the Office Action, Claims 1-18 were pending in this Application. Claims 1-6 and 18 have been withdrawn by Applicants due to an election/restriction requirement. Claims 7-17 are rejected. Applicants have amended Claim 7, and respectfully request reconsideration and favorable action in this case.

#### **Claim Objections**

Claim 7 was objected to by the Examiner for containing typographical errors. Applicants amend Claim 7 to overcome this objection and respectfully request full allowance of Claim 7 as amended.

#### **Claim Characterization**

On Page 3 of the Office Action, the Examiner provides a characterization of the claims including the statement "The claimed cardioplegia solution does not comprise NaCl, KCl, glucose, insulin, CaCl<sub>2</sub> and lidocaine." The cardioplegia solution in Claim 7 actually does comprise each of these ingredients. We assume for the purposes of this response that the sentence on Page 3 of the Office Action is a typographical error by the Examiner and should read "does comprise" instead of "does not comprise".

#### **Rejections under 35 U.S.C. § 112**

Claims 7-17 were rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite and failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The term "solution" after cardioplegia was missing in step ii) of Claim 7. As the Examiner correctly assumed, this "cardioplegia solution" is the same as that referenced throughout Claim 7 and its dependent claims. Applicants have amended Claim 7 to correct this error.

#### **Rejections under § 103**

Claims 7-17 were rejected by the Examiner under 35 U.S.C. § 103 as being unpatentable over Hans-Peter Hermann et al.'s "*Haemodynamic effects of intracoronary pyruvate in patients with congestive heart failure: an open study*" (hereinafter "Hermann").

Applicants respectfully traverse and submit that Hermann does not teach or suggest the present invention and, in fact, teaches away from the present invention.

A finding of obviousness under 35 U.S.C. §103(a) requires a demonstration of the scope and content of the prior art, the level of ordinary skill in the art, differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The relevant inquiry is whether the prior art both suggests the invention and provides one of ordinary skill in the art with a reasonable expectation that the suggestion would work. *In re O'Farrell*, 853 F.2d 1549, 7 USPQ2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be found in the prior art and not in Applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully submit that the differences between Hermann and the present application are much greater than the Examiner alleged. Essentially, the Examiner's entire argument is based on the premise that Hermann discloses a process for performing cardiopulmonary bypass surgery. In fact, Hermann has nothing to do with cardiopulmonary bypass surgery. Instead Hermann relates to a method of improving heart performance of congestive heart failure patients by supplying pyruvate through an arterial catheter. In addition, the goal in Hermann is to increase cardiac performance. The goal of the present invention is to stop the heart from beating and protect it while it is stopped. If Hermann accomplished the same goal as the present invention, he would have killed his patients.

More specifically, Hermann relates to "the effect of intracoronary pyruvate in patients with congestive heart failure". Hermann, p. 1321, Col. 1, Background. More specifically, Hermann "investigated the haemodynamic response to pyruvate in patients with congestive heart failure due to dilated cardiomyopathy." Hermann, p. 1321, Col. 2, Introduction. This was accomplished by cardiac catheterisation through the femoral artery and not through actual surgery. Hermann, p.1321, Col.1, Methods. The treatment resulted in "increased stroke volume index and decreased pulmonary capillary wedge pressure in each patient."

In contrast, the cardioplegia solution of the present invention is administered during cardiopulmonary bypass surgery. Claim 7. Such surgeries involve opening the chest cavity and stopping the heart from beating by introducing a cardioplegia solution. See Specification, Paragraph 0002. A cessation of the heartbeat is in direct contrast to the

increase in stroke-volume index (essentially the amount of blood the heart pumps out with each beat) observed in Hermann.

Furthermore, there is no suggestion in Hermann that its solution or anything like its solution be applied in a situation where the heart should stop beating. If anything, one would assume that Hermann's results, which show increased heart function, would indicate that the Hermann solution might serve poorly in a context where heart function is intended to stop, such as cardiopulmonary bypass surgery. Therefore, the present Claims are not obvious in light of Hermann.

Claims 7-17 were rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over PCT Publication No. WO 93/02653 filed by Leigh Segel (hereinafter "Segel") taken with:

- a. Vivek Rao et al.'s *"Insulin Cardioplegia for Elective Coronary Bypass Surgery"* (hereinafter "Rao"),
- b. U.S. Patent 4,988,515 issued to Gerald D. Buckberg (hereinafter "Buckberg"),
- c. Hermann et. al., and
- d. M. Isabel Tejero-Taldo et al.'s *"Antioxidant Properties of Pyruvate Mediate its Potentiation of  $\beta$ -Adrenergic Inotropism in Stunned Myocardium"* (hereinafter "Tejero-Taldo").

As the Examiner notes, Segel does not specifically disclose a cardioplegia solution containing pyruvate. Rather, Segel discloses a cardioplegia solution containing dextrose. Segel, Pages 19-20, Example C. The Examiner also notes that a "Crystalloid Solution" is disclosed that does include pyruvate. Segel, Page 11, Table 1. However, Applicants submit that it is far from clear that this "Crystalloid Solution" in Table 1 is the same as that used in the cardioplegia solution of Example C. The primary indicator that the two may not be the same is the recitation of dextrose as the energy source in the cardioplegia of Example C. Dextrose is not listed as a "Metabolic Substrate" or for any other reason in Table 1.

Furthermore, the Examiner indicates that Segel discloses "administering directly to the heart of a human patient a composition or a cardioplegia solution..." comprising pyruvate. It is fairly clear that Segel is merely reciting the steps for cardiopulmonary bypass surgery recited in Khuri et al. Segel, Page 19, Example C. Segel does not appear to have actually

used any of the cardioplegia's disclosed therein in an actual human test. Absent data showing functionality in a human test, it is not clear that the cardioplegia would have the desired effects. As the present application points out, even guinea pig data is not sufficient to indicate that a cardioplegia is functional. Specification, Paragraph 0013. Lack of any data is certainly not sufficient. The Buckberg patent suffers from the same deficiency. Buckberg provides data using a glucose and/or dextrose cardioplegia.

Furthermore, Hermann cannot be relied upon to provide a reasonable expectation of success because it relates to an entirely different type of treatment than the present invention. Similarly, Tajero-Taldo does not provide a reasonable expectation of success because it relates to a method of increasing cardiac output rather than stopping the heart and it uses guinea pigs, which are not always indicative of results in humans. Additionally, Tajero-Taldo uses isolated hearts which are often not indicative of hearts in real patients. Specification, Paragraphs 0011, 0013 and 0015.

Accordingly, the Segel and Buckbern references alone or in combination fail to disclose a cardioplegia containing pyruvate or, alternatively, fail to provide any data showing such a cardioplegia is functional in a human. Hermann and Tajero-Taldo fail to provide a reasonable expectation of success for a pyruvate-containing cardioplegia. Therefore, Applicants' Claims are not obvious in light of these references.


**CONCLUSION**

For the foregoing reasons, Applicants request that Claims 7-17 be allowed. Early and favorable acceptance of this application is respectfully requested.

Applicants believe no fee is due with this timely response. The Commissioner is hereby authorized to charge any fees or credit any overpayment to Deposit Account No. 02-0384 of Baker Botts L.L.P.

Respectfully submitted,

BAKER BOTTS L.L.P.

  
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